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Pregnancy in women after coronary revascularization

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Abstract

Pregnancy after coronary revascularization presents unique challenges to the management of antiplatelet therapy, anesthesia and mode of delivery. We present two cases where women of reproductive age required coronary revascularization with drug eluting stents after a myocardial infarction, and discuss key aspects of pregnancy and labor management.

Keywords

Cardiology, high-risk pregnancy, maternal–fetal medicine, drugs (medication)

Introduction

Coronary artery disease (CAD) remains the leading cause of mortality for women worldwide.[1] As pregnancy rates in older women continue to rise, with the 2012 birth rate for women aged 40–44 the highest reported in 33 years,[2] CAD management will impact women who may conceive after a cardiac event.[3]

We present two cases where women of reproductive age required coronary revascularization with drug eluting stents (DES) after a myocardial infarction (MI) soon after conception, raising important considerations during pregnancy about management of antiplatelet therapy, anaesthesia and mode of delivery. Consent from both patients to describe their medical and pregnancy history in a case report was obtained.

Case series

A 36 year old Caucasian female Gravida 7 Para 5015 with essential hypertension, supraventricular tachycardia and a 30 year pack smoking history presented at 10 weeks gestation for consultation. The patient had experienced an acute inferior wall ST elevation MI within 31 days of her last menstrual period. She underwent two percutaneous coronary interventions with everolimus DES to the left anterior descending and circumflex arteries. During a readmission for chest pain 5 weeks later, urine pregnancy test was positive and ultrasound revealed a 9 week gestation. Medications included metoprolol 50 mg twice daily, aspirin 325 mg daily and clopidogrel 75 mg daily. Simvastatin and lisinopril had been discontinued. Obstetric history included a 32 week delivery due to pre-eclampsia and four full-term vaginal deliveries, the last complicated by pre-eclampsia.

Aspirin was reduced to 81 mg daily and clopidogrel was continued, both through labour. Labour was induced at term due to gestational hypertension. She delivered vaginally without regional anesthesia a healthy male weighing 3420 g with normal Apgar scores. Patient underwent hysteroscopic sterilization 4 months postpartum and both mother and infant are doing well.

A 41 year old Caucasian female Gravida 1 with a 20–30 pack year smoking history and 9 years of infertility presented with a history of an acute inferior ST elevation MI 10 weeks before conception. Screening for antiphospholipid antibodies had been negative. She underwent everolimus DES placement to the right coronary and mid left anterior descending arteries. Discharge medications included aspirin 325 mg daily, clopidogrel 75 mg daily, metoprolol 12.5 mg twice daily, lisinopril 2.5 mg daily and simvastatin 85 mg daily. She had 3 months of amenorrhea within 6 months of the MI and was 17 weeks pregnant upon first presentation. Lisinopril, simvastatin and metoprolol were discontinued; dual antiplatelet therapy (DAPT) was continued. Oligohydramnios prompted delivery at 38 weeks gestation. Patient opted for an elective cesarean under general anesthesia since she desired not to deliver vaginally without regional anesthesia. She delivered a healthy female infant weighing 3925 g with normal Apgar scores. Postoperatively she had a wound hematoma with separation and anemia requiring 2 units of packed red blood cells.

Discussion

During pregnancy there is a 50% increase in intravascular volume, a decrease in systemic vascular resistance, an increase in the baseline heart rate and changes in coagulation, anticlotting and antifibrinolytic factors.[3,4] With these changes and the marked fluctuations in cardiac output,[5] women with underlying cardiac disease (prior cardiac event or arrhythmia, poor New York Heart Association functional class, left heart obstruction, or reduced systemic ventricular systolic function) may not tolerate pregnancy or delivery.[6]

Antepartum concerns for our patients included their functional status, normal for both, and their medications. Angiotensin-converting enzyme (ACE) inhibitors are contraindicated in the second and third trimesters as they have been linked to fetal hypocalvaria, oligohydramnios and renal defects.[7,8] Beta-blockers such as metoprolol and labetalol are commonly used during pregnancy; atenolol has been linked to intrauterine growth restriction when given early in pregnancy.[8–10] DAPT involves aspirin and clopidogrel. Chronic or intermittent high doses of aspirin may increase the risk of hemorrhage[7] and may lead to premature closure of the ductus arteriosus in the third trimester. However, low dose aspirin is used during pregnancy for pre-eclampsia

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prevention or in antiphospholipid antibody syndrome.[11] Clopidogrel, a direct inhibitor of adenosine diphosphate-induced platelet aggregation, is indicated for reducing atherosclerotic events after an MI or stroke. Although not teratogenic in animal studies, clopidogrel reports in human pregnancy are limited.[7,12–14]

Intrapartum concerns for patients with DES on DAPT include delivery and anaesthesia. While both bare metal stents (BMSs) and DESs prevent restenosis by attenuating early arterial recoil and contraction,[15] DES further prevent restenosis by delivering drug locally to the arterial narrowing. Both stent types require lifelong aspirin but DES require an additional 6–12 months of additional antiplatelet therapy with clopidogrel or newer agents such as ticagrelor and prasugrel, compared to 1 month of DAPT with BMS. Early cessation of DAPT in stent patients increases the risk of stent thrombosis, which carries a high risk of major MI or death.

Several reports describe pregnant women whose clopidogrel was discontinued 7–10 days prior to delivery.[12,14] A woman with essential thrombocythemia had undergone aortocoronary bypass grafting after an MI and was on clopidogrel until 10 days before delivery.[12] Low molecular weight heparin was administered during the week before delivery and on day of induction. She delivered vaginally without regional anesthesia. A second patient had a DES, was managed on DAPT until 1 week before delivery and delivered via caesarean without complications.[14] Two reports describe pregnant women who experienced acute coronary syndrome managed with clopidogrel.[16,17] Delivery information is unavailable for the first case.[16] In the second case, aspirin and clopidogrel were held the morning of the planned caesarean performed for fetal indications.[17] A woman at 28 weeks gestation underwent revascularization with DES, treatment with clopidogrel and was delivered by caesarean due to concerns for regional anesthesia while on DAPT.[18] The patient received enoxaparin 40 mg the evening before surgery; aspirin and clopidogrel were held the morning of surgery.[18]

In a recent report, a woman conceived within 2 months of DES placement while on clopidogrel and aspirin.[13] Aspirin was discontinued but clopidogrel was continued during pregnancy. The patient was delivered by caesarean for fetal indications under general anesthesia and experienced postoperative bleeding requiring a transfusion. A single case report on aspirin and prasugrel during pregnancy found no complications for mother or neonate.[19]

Our case report contributes to the limited literature addressing women who conceive soon after coronary revascularization with DES.[13] With DAPT, pregnancy concerns include medication exposure, anaesthesia and bleeding risks with either vaginal or caesarean birth. Cardiologists remain concerned about stopping antiplatelet therapy due to the concern for stent thrombosis with highest risk of stent thrombosis early before the stent has endothelialized. Women who conceive after BMS placement are managed with aspirin and 1 month of additional antiplatelet therapy, whereas women who conceive soon after DES placement are generally continued on DAPT given the concern for stent thrombosis. Although recent literature suggests that DAPT after zotarolimus-eluting stents could be limited to 3–6 months,[20] for patients delivering 3–6 months after DES placement, decisions to hold clopidogrel and other agents are individualized. However, the optimal duration of antiplatelet therapy remains in question[21] and not enough information is available to suggest changes in women who conceive soon after DES placement. Although some suggest these agents can be held and delivery considered on just aspirin alone, the attendant risks of stent thrombosis off DAPT in DES patients far outweigh the risks of bleeding and careful counselling is advised.

As women delay childbearing, pregnancy testing should be routine when evaluating women with chest pain, although emergently, coronary revascularization should not be delayed. Once revascularization has taken place, contraception avoiding estrogen should be encouraged for at least 12 months. For women who conceive after revascularization, a multidisciplinary care team including perinatology/obstetric medicine, cardiology and anaesthesia is advised.

Declaration of conflicting interests

None declared

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Ethical approval

Written consent was obtained from both patients described in the case report. Approval by our Institutional Review Board was not obtained as this is not applicable for purposes of our case report.

Guarantor

The guaranteeing author for this paper is Joanne N Quiñones, MD, MSCE. Dr Quiñones guarantees the manuscript's accuracy and the contributorship of all co-authors.

Contributorship

Dr Quiñones wrote the manuscript with the assistance of Drs Cox, Smolinski, Coassolo, Maksimik and Freudenberger. Dr Quiñones, Smolinski, Maksimik and Coassolo also directly cared for the patients described in the case report. All above authors meet the conditions of authorship and each author participated sufficiently in the work to take public responsibility for appropriate portions of the content.

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